

Amendments to the Specification:

Please replace the paragraph beginning at page 13, line 24 with the following amended paragraph:

An example of computer instructions to perform the steps above is provided by breed.py, shown in the Appendix. These instructions use the OEChem Python toolkit (OpenEye Scientific Software, Inc.) and the Python programming language (Python Software Foundation, [www.python.org](http://www.python.org) ~~www.python.org~~). The instructions can be compatible with, for example, version 1.0 or version 1.1 beta of OEChem. One of skill in the art can adapt the instructions to be compatible with alternate version of OEChem.

Please replace the paragraph beginning at page 22, line 28 with the following amended paragraph:

The steps of the ligand breeding methods, which can include both steps implemented by commercially available software packages, and steps implemented by instructions to perform the breeding function (e.g., breed.py) can be integrated using instructions provided with a scripting language (e.g., Perl<sup>TM</sup>, Python<sup>TM</sup>), or a compiled language (e.g., C, Fortran).

Please delete previous abstract at page 43 and add the following new abstract:

Methods of and devices directed to generating a target ligand are disclosed herein. The methods can include, for example, providing a set of models, wherein each model comprises three-dimensional structural information for a ligand or a ligand:macromolecule complex, wherein each ligand comprises a plurality of atoms and a plurality of bonds, and wherein each model is related to the other models of the set by a homologous structural feature; mapping spatial relationships between the models such that the models are superimposed with respect to the homologous structural feature; identifying one or more pairs of matching bonds between ligands of the set, wherein the matching bonds comprise a bond of a first ligand (B1) and a bond of a second ligand (B2) that are superimposed such that (i) an atom at each end of the bond (B1)

is within 1.8 angstrom of an atom at each end of the bond (B2), (ii) the bond (B1) and the corresponding bond (B2) are of the same bond order, and (iii) the bond (B1) and the corresponding bond (B2) are related by an angle of 30° or less; selecting a plurality of subsets of atoms and/or bonds from each ligand; wherein each subset comprises a bond and/or, an atom connected to a matching bond; generating and displaying output ligands, each output ligand comprising atoms and/or bonds of a first subset and atoms and/or bonds of a second subset, wherein the first subset and the second subset comprise atoms and/or bonds derived from opposite ends of the a matching bond.